

Leukaemia Diagnosis Interpretation

All Participants

Participant: 42981

Trial No: 161704

Date Issued: 14-November-2016

Closing Date: 02-December-2016

Trial Comments

This was an electronic only trial issued to a total of 798 participants.
Please note - From this trial forward the classification of diagnoses has changed.
Please see the additional information in the attached conclusion.

Your Diagnosis: Sezary syndrome

Consensus Diagnosis: Sezary syndrome

Your Diagnosis is classed as being **CORRECT DIAGNOSIS** (on rare occasions this may not be the consensus diagnosis).

Performance Score: 0

Running Score: 50

Consensus

	Consensus Diagnosis	Your Diagnosis
Lineage	Lymphoid T cell	Lymphoid T cell
Subclassification	Mature T-cell and NK-cell neoplasms	Mature T-cell and NK-cell neoplasms
Diagnosis	Sezary syndrome	Sezary syndrome

Breakdown of returned diagnoses

Diagnosis	No Of Returns	Percentage Of Returns
Total Returns	324	100.0
Sezary syndrome	236	72.8
T-cell prolymphocytic leukaemia	30	9.3
Peripheral T-cell lymphoma, NOS	27	8.3
T lymphoblastic leukaemia/lymphoma (NOS)	12	3.7
Adult T-cell leukaemia/lymphoma	9	2.8
Mycosis fungoides	5	1.5
Early T-cell precursor lymphoblastic leukaemia (Provisonal entity)	3	0.9
Primary cutaneous CD4 positive small/medium T-cell lymphoproliferative disorder	2	0.6

Issue Date: 24 Jan 2017

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LDI 161704 1.0.0

Sheffield Teaching Hospitals NHS Foundation Trust, a UKAS proficiency testing provider No. 7804, operating UK NEQAS for Leucocyte Immunophenotyping.

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Version: 1.01

Leukaemia Diagnostic Interpretation trial 161704

Important notice regarding changes to diagnosis classification for the Leukaemia Diagnostic Interpretation programme

The diagnosis of haematological malignancy has evolved in the last few decades aided by the greater understanding of the genetic basis of oncogenesis. Today the tools developed during that era, including monoclonal antibodies, genetic probes used in hybridisation and amplification techniques through to next generation sequencing techniques, can all be utilised in the classification of haematological neoplasms. Indeed the detection of specific genetic markers can completely change the immediate treatment and outcome of patients.

The results of these investigations are now incorporated into the extensive descriptions that underpin the disease classifications described in the 'WHO Classification of Tumors of Haemopoietic and Lymphoid Tissues' a classification which has been adopted worldwide as the defining criteria for establishing the diagnosis of haematological neoplasms.

UK NEQAS LI and the steering committee have been committed to developing quality assessment schemes that would not only allow laboratories and diagnosticians to benchmark the results of their analyses with others, but also to develop schemes that would allow the incorporation of all testing modalities in developing an overall diagnosis. UKNEQAS LI now runs various QA schemes for leucocyte immunophenotyping and molecular analysis. However these schemes have a necessity to develop and evolve so that they can provide laboratories with useful tools that can be used to prove accuracy and competence in the tasks that they undertake and provide for the patients that they serve.

UK NEQAS LI and the steering committee believe that the Leukaemia diagnostic interpretation scheme now needs to evolve to drive greater diagnostic accuracy within the field. Greater accuracy in the diagnosis of haematological neoplasms is in part the subject of the National Institute for Health and Care Excellence (NICE) publication Haematological cancers: improving outcomes (Published May 2016 available at <https://www.nice.org.uk/guidance/ng47>) which mandates the use of integrated technologies and multi-disciplinary teams to review all diagnoses of haematological neoplasm's in the UK.

The steering committee has recommended that the scoring scheme used for the assessment of the Leukaemia diagnostic interpretation be changed to three new categories;

- The **Correct Diagnosis** - This will be established by an expert panel/committee from all of the data provided including; clinical presentation, morphology, immunophenotype, cytogenetic and molecular genetic data. On rare occasions this may not be the consensus diagnosis.

- A **Differential Diagnosis** classification is such that the diagnosis is deemed plausible in the absence of further pathological tests, and the majority of the Expert Committee is in agreement. If your diagnosis falls into this category you will not be penalised.
- The classification of an **Incorrect Diagnosis** is one that does not utilise all of the available information to establish either the correct or differential diagnosis. It could also be a diagnosis that may lead clinicians to give sub-optimal therapy. This classification would also be used where a submitted diagnosis has either assumed or introduced pathologies other than those provided in the trial data set e.g. stating there is a t(15;17).
- A non return of results will be classed as an **Incorrect Diagnosis** and scored accordingly.

By making these changes the steering committee believe that the scheme will remain fit for purpose and can be used as part evidence for proving competency to regulatory bodies such as UKAS/CAP etc.

Clinical History/Information

45 year old male patient presented with generalised erythroderma and increased pruritus.

Haematological examination revealed the following:

Hb - 133 g/L; WBC – $183.5 \times 10^9/L$; PLT - $390 \times 10^9/L$; RBC – $4.4 \times 10^{12}/L$; HCT - 0.4 L/L; MCV – 91.2 fL; MCH – 30.0 pg; Lymphocytes – $172.5 \times 10^9/L$

Immunophenotype

CD3+, CD4+, CD5+, CD45+, TCRαβ+. There was reduced expression of CD2 and CD7

All other antigens were negative

Peripheral Blood Morphology

Morphology comments from Professor Wendy Erber

Consultant Haematologist, University of Western Australia, Nedlands, Australia

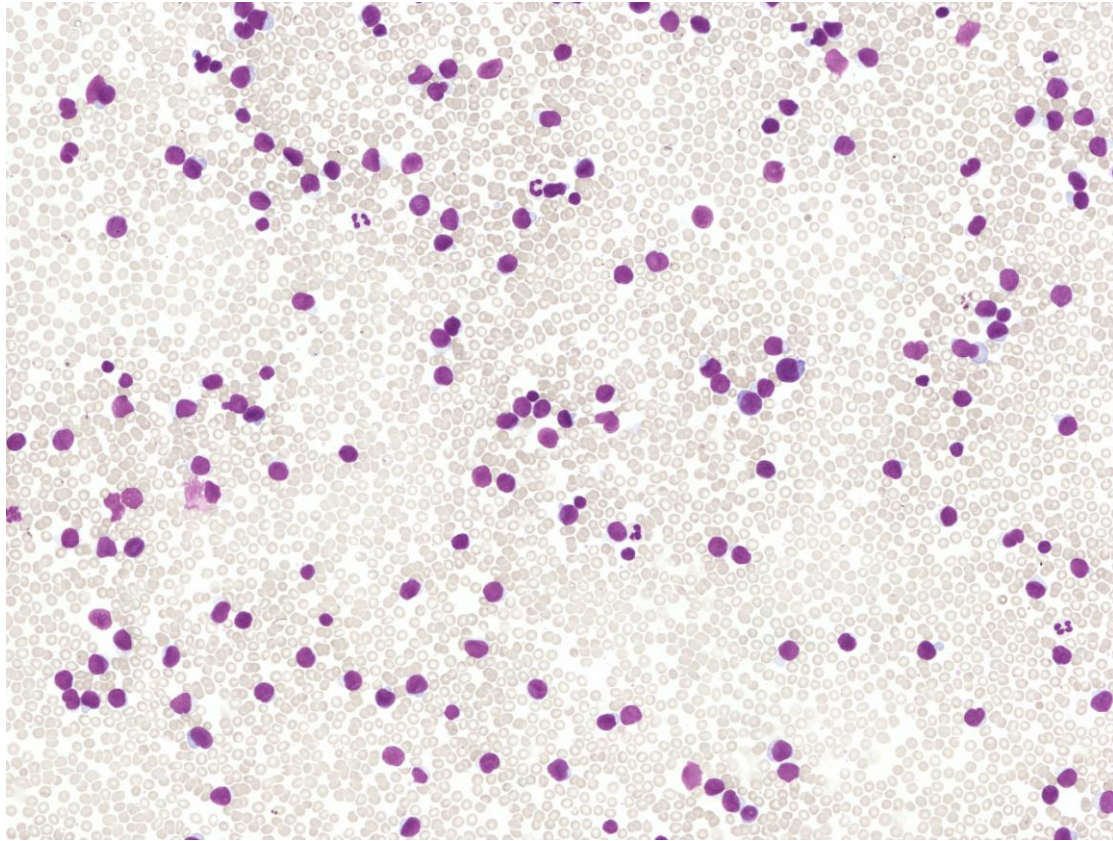
COMMENT:

The blood film shows a marked leucocytosis comprised of intermediate to large sized mononuclear cells with a high nuclear:cytoplasmic ratio. The nuclei are large and predominantly round. Many have a nuclear groove or are cerebriform. The chromatin varies from fine (the majority) to coarsely clumped; there are no nucleoli. The cells have minimal cytoplasm. Some smaller cells with comparable morphology are present.

Diagnosis: Morphology is consistent with Sézary Syndrome

Example of Digital Images Issued

Figure 1: Peripheral Blood x50 magnification (May Grünwald Giesma stain)



Cytogenetics and Molecular genetics

Analysis has shown this patient to have an XY sex chromosome constitution and a complex chromosome abnormalities present in a mosaic state (in 70%-90% of cells), as well as partial chromosomal losses and gains present in a mosaic and non mosaic state.

Numerical abnormalities identified included:

monosomy 6 (approx 40% of cells); trisomy 7 (approx 30% of cells); trisomy 8 (approx 30% of cells); monosomy 10p14q26.3 (in >90% of cells); monosomy 11 (approx 40% of cells); monosomy 12p13.1q24.33 (approx 40% of cells); trisomy 17p11.2q25.3 (most likely consistent with isodicentric 17q in 70% of cells); monosomy 22 (approx 30% of cells). Furthermore, non-mosaic, copy number neutral isodisomy of chromosome 9 was detected.

DNA copy number changes identified included loss of 1p, 2p, 3p, 3q, 9p, 12p, 14q, 16q, 17p, 19p and gain of 10p. Clonal TCR (β and γ) gene rearrangements were detected by PCR.

Exercise Conclusion / Case Discussion

Please note that, because this trial requires a diagnosis based on the WHO guidelines, this report is therefore based on the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th Edition¹, The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukaemia² and The 2016 revision to the World Health Organization classification of lymphoid neoplasms³.

Finding from Leukaemia Immunophenotyping - Part one

There were no significant findings.

Leukaemia Diagnostic Interpretation - Part Two

Submitted Diagnoses:

Please note:

- The consensus diagnosis may not necessarily be viewed as the correct diagnosis as determined by the Steering Committee. If your diagnosis falls into this category you will not be penalised.
- A differential diagnosis classification is such that the diagnosis is plausible in the absence of further pathological tests, and the majority of the Steering Committee is in agreement. This category may also contain the working diagnosis. If your diagnosis falls into this category you will not be penalised.
- The classification of an incorrect diagnosis is where the participant has submitted a diagnosis that would have a major therapeutic effect or has assumed/introduced pathologies to be present other than those provided in the clinical history e.g. stating there is a t(15;17), or if the Steering Committee has stated that the diagnosis is incorrect.

Consensus Diagnosis

Sézary syndrome

The phenotype, morphology, complex karyotype and clinical presentation are all consistent with this diagnosis

Differential Diagnoses

T-cell prolymphocytic leukaemia

This has been classed as a differential diagnosis based on the caveat that the Steering Committee was split in its classification. It would normally be classed as incorrect but the high WCC may have pushed participants towards this diagnosis. Cases of TPLL are characterised by strong expression of CD7, with normal expression of other T cell markers. The morphology is not consistent with this disease and cytogenetically, an inversion at q11 and q32 is seen in

80% of cases. The majority of patients present with hepato-splenomegaly. This was not reported in this case

Peripheral T-cell lymphoma, NOS

Patients usually present with peripheral lymph node enlargement. There is sometimes peripheral blood involvement but leukaemic presentation is rare. The phenotype, morphology and cytogenetics are not consistent with the disease.

Mycosis fungoides

This disease accounts for 50% of primary cutaneous T cell lymphomas. Although it is usually limited to the skin, extracutaneous dissemination to the lymph nodes, liver, spleen, lungs and blood can occur in advanced stages. The phenotype is consistent with Mycosis fungoides. Morphologically, when the cells circulate in the blood, they are known as Sezary cells.

Incorrect Diagnoses

T lymphoblastic leukaemia/lymphoma (NOS)

Cases of TALL usually express TDT and have variable expression of CD1a, CD2, CD3, CD4, CD5 and CD8. Cytoplasmic CD3 and CD7 are commonly positive.

Adult T-cell leukaemia/lymphoma

This is an incorrect diagnosis based solely on the fact that this disease is associated with HTLV-1 retroviral infection. This information was not provided in the clinical history/information and is therefore incorrect.

Early T-cell precursor lymphoblastic leukaemia (Provisional entity)

Phenotypically, cases are cytoplasmic CD3 positive and surface CD3 negative and classically express one or more myeloid antigens. CD5 is often negative.

Primary cutaneous CD4 positive small/medium T-cell lymphoproliferative disorder

Patients with this lymphoma can present with skin infiltration although these are often solitary lesions. Cases often show the loss of expression of T cell antigens.

Further Trial Findings

Table 1: Submissions from all participants - laboratories and individuals.

Diagnosis	Total No. of Returns	No. of Laboratories	No. of Individual
Sézary syndrome	236	161	75
T-cell prolymphocytic leukaemia	30	17	13
Peripheral T-cell lymphoma, NOS	27	18	9
T lymphoblastic leukaemia/lymphoma (NOS)	12	6	6
Adult T-cell leukaemia/lymphoma	9	7	2
Mycosis fungoides	5	2	3
Early T-cell precursor lymphoblastic leukaemia (Provisional entity)	3	1	2
Primary cutaneous CD4 positive small/medium T-cell lymphoproliferative disorder	2	0	2

Table 2: Submissions from laboratory participants only

Diagnosis	Laboratory Returns %
Sézary syndrome	75.9
T-cell prolymphocytic leukaemia	8.0
Peripheral T-cell lymphoma, NOS	8.5
T lymphoblastic leukaemia/lymphoma (NOS)	2.8
Adult T-cell leukaemia/lymphoma	3.3
Mycosis fungoides	1.0
Early T-cell precursor lymphoblastic leukaemia (Provisional entity)	0.5

Table 3: Submissions from individual participants only

Diagnosis	Individual Returns %
Sézary syndrome	67.0
T-cell prolymphocytic leukaemia	11.6
Peripheral T-cell lymphoma, NOS	8.0
T lymphoblastic leukaemia/lymphoma (NOS)	5.4
Adult T-cell leukaemia/lymphoma	1.8
Mycosis fungoides	2.7
Early T-cell precursor lymphoblastic leukaemia (Provisional entity)	1.8
Primary cutaneous CD4 positive small/medium T-cell lymphoproliferative disorder	1.8

Reference:

1. Steven H. Swerdlow, Elias Campo, Nancy Lee Harris, Elaine S Jaffe, Stefano A. Pileri, Harald Stein, Jürgen Thiele, James W. Vardiman. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th Edition. IARC Press 2008
2. Daniel A. Arber, Attilio Orazi, Robert Hasserjian, Jürgen Thiele, Michael J. Borowitz, Michelle M. Le Beau, Clara D. Bloomfield, Mario Cazzola, James W. Vardiman. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukaemia. Blood 2016;127(20) 2391-2405
3. Steven H. Swerdlow, Elias Campo, Stefano A. Pileri, Nancy Lee Harris, Harald Stein, Reiner Siebert, Ranjana Advani, Michele Ghielmini, Gilles A. Salles, Andrew D. Zelenetz, Elaine S Jaffe. The 2016 revision to the World Health Organization classification of lymphoid neoplasms. Blood 2016;127(20) 2375-2390

Information with respect to compliance with standards BS EN ISO/IEC 17043:2010

4.8.2 a) The proficiency testing provider for this programme is:

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4.8.2 b) The coordinators of UK NEQAS LI programmes are Prof David Barnett and Mr Liam Whitby.

4.8.2 c) Person(s) authorizing this report:

Prof David Barnett, Director or Mr Liam Whitby, Operations Manager of UK NEQAS LI

4.8.2 d) No activities in relation to this EQA exercise were subcontracted.

4.8.2 g) The UK NEQAS LI Confidentiality Policy can be found in the Quality Manual which is available by contacting the UK NEQAS LI office. Participant details, their results and their performance data remain confidential unless revealed to the relevant NQAAP when a UK participant is identified as having performance issues.

4.8.2 i) All EQA samples are prepared in accordance with strict Standard Operational Procedures by trained personnel proven to ensure homogeneity and stability. Where appropriate/possible EQA samples are tested prior to issue. Where the sample(s) issued is stabilised blood or platelets, pre and post stability testing will have proved sample suitability prior to issue.

4.8.2 l), n), o), r) & s) Please refer to the UK NEQAS LI website at www.ukneqasli.co.uk for detailed information on each programme including the scoring systems applied to assess performance (for BS EN ISO/IEC 17043:2010 accredited programmes only). Where a scoring system refers to the 'consensus result' this means the result reported by the majority of participants for that trial issue. Advice on the interpretation of statistical analyses and the criteria on which performance is measured is also given. Please note that where different methods/procedures are used by different groups of participants these may be displayed within your report, but the same scoring system is applied to all participants irrespective of method/procedure used.

4.8.2 m) We do not assign values against reference materials or calibrants.

4.8.2 q) Details of the programme designs as authorized by The Steering Committee and Specialist Advisory Group can be found on our website at www.ukneqasli.co.uk. The proposed trial issue schedule for each programme is also available.

4.8.2 t) If you would like to discuss the outcomes of this trial issue, please contact UK NEQAS LI using the contact details provided. Alternatively, if you are unhappy with your performance classification for this trial, please find the appeals procedure at www.ukneqasli.co.uk/contact-us/appeals-and-complaints/